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EXAMINER	
KUMAR, VINOD	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,515	BRUGLIERA ET AL.	
	Examiner	Art Unit	
	VINOD KUMAR	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *92-115* is/are pending in the application.

4a) Of the above claim(s) *114 and 115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *92-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 July 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/17/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of objections and rejections

1. Applicant's response filed in the paper of September 17, 2008 is entered.

2. Claims 1-91 are canceled and claims 92-115 are newly added claims.

3. Newly added claims 92-113 fall within the scope of the elected invention, and are thus examined on merits in the present examination.

4. Newly added claims 114-115 have been withdrawn because they fall within the scope of non-elected invention.

5. Objections to the specification are withdrawn in light of amendment to the specification filed in the paper of September 17, 2008.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. All previous claim objections and rejections not set forth below have been withdrawn in light of claim amendments filed in the paper of September 17, 2008.

Election/restriction

8. Newly added claims 114-115 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 5, 2007. The restriction was made FINAL.

This application contains claims 114-115, drawn to an invention nonelected with traverse in the reply filed on December 5, 2007. A complete reply to the final rejection

must include cancellation of nonelected claim or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

9. Initialed and dated copy of Applicant's IDS form 1449 filed in the paper of September 17, 2008 is attached to the instant Office action. The submission is in compliance with the provisions of 37 CFR 1.97.

Accordingly, the information disclosure statement is being considered by the examiner. However, it must be noted that Non-Patent Literature (NPL) cited as item # 6 is crossed because the cited reference has been included in PTO 892 of the last Office action.

Oath/Declaration

10. The oath or declaration remains defective because non-initialed and/or non-dated alteration to the address of inventor "Ronald Koes" has been made to the oath or declaration filed in the paper of May 27, 2005. See 37 CFR 1.52(c).

A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. Also see MPEP § 602.07 and MPEP § 1893.01.

In the response filed in the paper of September 17, 2008, Applicant states that a new oath will be submitted soon. Accordingly, the objection is maintained.

Claim Objections

11. Newly added claim 103 is objected to because of the following informalities:

Newly added claim 103 is objected for reciting "mutant" instead of "material" in line 3.

Claim Rejections - 35 USC § 112

12. Newly added claims 97-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 97-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because claims 97-99 recite the limitation "molecule" after "anthocyanin". There is insufficient antecedent basis for this limitation in these claims.

13. Claims 92-115 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleotide sequence encoding a flavonoid methyltransferase (FMT) including the one defined in SEQ ID NO: 12, a genetic construct or a genetically modified plant comprising said nucleotide sequence, does not

reasonably provide enablement for (a) a nucleotide sequence having about 70% or 95% identity to SEQ ID NO: 11, (c) a nucleotide sequence encoding an amino acid having about 80% or 95% identity to SEQ ID NO: 12, and (d) a nucleotide sequence capable of hybridizing under medium stringency conditions to a nucleotide sequence encoding SEQ ID NO: 12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reasons of record stated for claims 70-89 (now canceled) in the Office action mailed March 17, 2008.

Applicant traverses the rejection in the paper filed September 17, 2008.

Applicant argues that based on the teachings provided in the specification, those skilled in the art would be able to make and use the nucleic acids presently claimed without undue experimentation (response, paragraph bridging pgs 11 and 12).

Applicant's arguments have been fully considered but are deemed to be unpersuasive.

Newly added claims 92, 100 and 103 are directed to a nucleotide sequence having at least about 70% sequence identity to SEQ ID NO: 11.

Newly added claims 92, 100 and 103 are also directed to a nucleotide sequence encoding a protein having at least about 80% sequence identity to SEQ ID NO: 12.

Newly added claims 93, 101 and 104 are also directed to a nucleotide sequence having at least about 95% identity to SEQ ID NO: 11.

Newly added claims 94, 102 and 105 are also directed to a nucleotide sequence encoding a polypeptide having 95% identity to SEQ ID NO: 12.

It is maintained that the instant specification, however, provides guidance for how to make and use a nucleotide sequence (SEQ ID NO: 11) encoding *Torenia hybrida* cv. Summerwave flavonoid methyltransferase (FMT) of SEQ ID NO: 12 (pgs 72-73, example 9). The specification teaches using said nucleotide sequence in a method of producing a transgenic rose plant having modified petal (flower part) color compared to a control plant (pgs 82-92, example 11, table 2). The specification also states that the methylated derivatives of delphinidin, malvidin, and petunidin were detected in the transgenic rose exhibiting modified flower color. The specification also states that peonidin, the methylated derivative of cyanidin was also detected in the flowers of the transgenic rose plant (paragraph bridging pages 92 and 93; pages 94-96, tables 21, 22, and 23).

The instant specification also fails to provide guidance on how to make nucleic acid sequences encoding a functional FMT protein having 70% or 95% sequence identity to SEQ ID NO: 12.

Making all possible single amino acid substitutions in an 239 amino acid long protein like that encoded by SEQ ID NO: 11 would require making and analyzing 19^{239} nucleic acid sequences; these proteins would have 99.5% identity to SEQ ID NO: 12.

Because nucleic acid sequences encoding proteins with 80% sequence identity to the 239 amino acid long SEQ ID NO: 12 would encode proteins with 48 amino acid substitutions relative to SEQ ID NO: 12, many more than 19^{239} nucleic acid sequences would need to be made and analyzed.

Because nucleic acid sequences encoding proteins with 95% sequence identity to the 239 amino acid long SEQ ID NO: 12 would encode proteins with 12 amino acid substitutions relative to SEQ ID NO: 12, many more than 19^{239} nucleic acid sequences would need to be made and analyzed.

The instant specification also fails to provide guidance on how to make nucleic acid sequences having 70% sequence identity to SEQ ID NO: 11, and which encode a functional FMT protein.

Nucleotide sequences with 70% identity to SEQ ID NO: 11 would have 301 substitutions relative to 1006 nucleotides of SEQ ID NO: 11; these encompass nucleotide sequences that encode proteins having 0% sequence identity to SEQ ID NO: 12.

Nucleotide sequences with 95% identity to SEQ ID NO: 11 would have 50 substitutions relative to 1006 nucleotides of SEQ ID NO: 11; these encompass nucleotide sequences that encode proteins having 79% sequence identity to SEQ ID NO: 12.

It is maintained that from the guidance in the specification, it would appear that a large number of amino acids in SEQ ID NO: 12 could be substituted with any other amino acid.

It is further maintained that the instant specification fails to provide guidance for which amino acids of SEQ ID NO: 12 can be altered and to which other amino acids,

and which amino acids must not be changed, to maintain flavonoid methyltransferase activity of the altered protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein having flavonoid methyltransferase activity.

It is further maintained that making amino acid substitutions in a functional flavonoid methyltransferase, such as the one defined as SEQ ID NO: 12 protein is unpredictable. While it is known that many amino acid substitutions, additions or deletions are generally possible in any given protein the positions within the protein's sequence where such amino acid changes can be made with a reasonable expectation of success (without altering protein function) are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see for example, Wells, Biochemistry 29:8509-8517, 1990, see pages 8511-8512, tables 1-2; Ngo et al., pp. 492-495,1994, see page 491, 1st paragraph).

Also see Guo et al. (PNAS, 101: 9205-9210, 2004, see page 9205, abstract; page 9206, table 1; page 9208, figure 1) who teach that there is a probability factor of 34% that a random amino acid replacement in a given protein will lead to its functional inactivation. In the instant case, such a probability factor will be much higher as the claims encompass more than a single amino acid changes of the polypeptide defined in SEQ ID NO: 12.

Also see, Keskin et al. (Protein Science, 13:1043-1055, 2004, see page 1043, abstract) who teach that proteins with similar structure may have different functions. Furthermore, Thornton et al. (Nature structural Biology, structural genomics supplement, November 2000, page 992, 2nd paragraph bridging columns 1 and 2) teach that structural data may carry information about the biochemical function of the protein. Its biological role in the cell or organism is much more complex and actual experimentation is needed to elucidate actual biological function under *in vivo* conditions.

Thus, making and analyzing proteins with a large number of amino acid changes that also have flavonoid methyltransferase activity would require undue experimentation.

Additionally, newly added claim 103 is directed to a genetically modified plant comprising a genetic material, comprising a nucleotide sequence selected from parts (i) to (vi) of claim 103, however, the genetic material comprises no promoter. The specification does not teach how to use such a plant if the genetic material is not expressed. The specification does not teach how to obtain altered flowers or inflorescence (see claim 109) in such a plant if the genetic material is not expressed. The specification also does not teach making a genetically modified plant having functional FMT (SEQ ID NO: 12) which methylates on anthocyanins in any manner other than transforming (introducing and overexpressing) a plant with a nucleotide acid sequence encoding the FMT protein of SEQ ID NO: 12.

Given the claim breath, unpredictability, and lack of guidance as discussed above, it is maintained that undue experimentation would have been required by one skilled in the art to develop and evaluate nucleotide sequences encoding proteins having about 80% or 95% sequence identity to SEQ ID NO: 12, and nucleotide sequences having about 70% or 95% sequence identity to SEQ ID NO: 11, for obtaining genetically modified plants having altered flower color and morphology (inflorescence) due to increase in methylated anthocyanin content. See Genentech, Inc. v. Novo Nordisk, A/S, USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Claims 92, 100 and 103 are directed to a nucleotide sequence capable of hybridizing under medium stringency conditions to SEQ ID NO: 11 or its complementary form. Claims 92, 100, and 103 are also directed to a nucleotide sequence capable of hybridizing under medium stringency conditions to the nucleotide sequence in parts (iv) or (v) of claims 92, 100 and 103.

This would imply that any nucleotide sequence would hybridize to a nucleotide sequence encoding the polypeptide of SEQ ID NO: 12. This is because the medium stringency conditions of hybridization recited in the claims would encompass hybridization of a nucleic acid sequence that is unrelated to a nucleotide acid sequence encoding SEQ ID NO: 12.

The medium stringency conditions of hybridization (also see page 28 of the specification) would imply that sequences, which do not encode a protein, or encode a

protein which is unrelated in function to SEQ ID NO: 12, would also hybridize under the medium stringency conditions to a nucleotide sequence encoding SEQ ID NO: 12.

State of the art related to DNA hybridization suggests that in order to prevent hybridization of unrelated nucleic acid sequence(s) to a target sequence, hybridization and subsequent washing conditions must be highly stringent. For example, hybridization under conditions of 0.1 - 1.0x SSC, 50% formamide and 50 °C for 24 hours, followed by 2 washes in 0.1% SDS, 0.1x SSC at 65 °C for 25-30 minutes each is considered highly stringent condition that would not allow hybridization of unrelated nucleic acid sequences to the target sequence. See for example, Maniatis et al. (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1982; see in particular pages 387-389).

In the absence of adequate guidance, it is maintained that undue experimentation would have been required by one skilled in the art at the time the claimed invention was made to determine how to use said unrelated sequences in obtaining methylated anthocyanins or derivatives thereof.

In the absence of guidance, it is maintained that undue experimentation would have been required by a skilled artisan to determine how to use genetic constructs or genetically modified plant cells or plants comprising said unrelated sequences in obtaining methylated anthocyanins which modify flower color.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to

develop and evaluate nucleic acids that hybridize under medium stringency conditions to a nucleotide sequence encoding SEQ ID NO: 12.

As the specification does not describe the transformation of any plant with a gene comprising a promoter operably linked with (a) a nucleotide sequence having 70% or 95% sequence identity to SEQ ID NO: 11, (b) a nucleotide sequence encoding a polypeptide having 80% or 95% identity to SEQ ID NO: 12, or (c) a nucleotide sequence (unrelated) hybridizing under medium stringency conditions to a nucleotide sequence encoding FMT of SEQ ID NO: 12, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those which produce functional FMT that can methylate anthocyanins and derivatives of anthocyanin substrate to modify flower color and/or morphology (inflorescence), if such plants are even obtainable. It is, therefore, maintained that given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

14. Claims 92-113 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the following phrases "70% identity after optimal alignment to SEQ ID NO:

11" (claims 92, 100 and 103), "95% identity after optimal alignment to SEQ ID NO: 11" (claims 93, 101 and 104), "80% identity after optimal alignment to SEQ ID NO: 12" (claims 92, 100 and 103) and "95% identity after optimal alignment to SEQ ID NO: 12" (claims 94, 102 and 104). The specification fails to provide support for these phrases. Thus, such phrases constitute NEW MATTER.

Applicant's response filed in the paper of September 17, 2008 cites pages 27-28 for the support. It is noted that page 27 of the specification states % similarity to the nucleic acid sequences of the invention. The cited pages do not describe the % identity as instantly claimed.

15. Newly added claims 92-113 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record stated for claims 70-89 (now cancelled) in the Office action of March 17, 2008. Applicant traverses the rejection in the paper filed September 17, 2008.

Applicant argues that the specification described a well-defined genus of molecules which are characterized by sufficient structural and functional features in a manner consistent with written description. Applicant provides no reasons to support these arguments (response, pg 12, 3rd paragraph).

Applicant's arguments have been fully considered but are deemed to be unpersuasive.

The essential feature of newly added claims 92, 100 and 103 is a nucleotide sequence encoding an amino acid sequence having at least about 80% sequence similarity to SEQ ID NO: 12. The essential feature of newly added claims 92, 100 and 103 is also a nucleotide sequence having at least about 70% sequence identity to SEQ ID NO: 11.

The essential feature of newly added claims 94, 102 and 105 is a nucleotide sequence encoding an amino acid sequence having at least about 95% sequence similarity to SEQ ID NO: 12. The essential feature of newly added claims 93, 101 and 104 is also a nucleotide sequence having at least about 95% sequence identity to SEQ ID NO: 11.

The specification, describes the structure of a nucleotide sequence (SEQ ID NO: 11) encoding FMT protein of SEQ ID NO: 12. The specification also describes the function of modifying flower color in a transgenic plant overexpressing said nucleotide sequence (pgs 72-73, example 9; pgs 82-92, example 11, table 2).

Nucleotide sequences encoding structures (proteins) having about 80% or 95% sequence identity to instant SEQ ID NO: 12 are no described, and thus their function is unknown.

Nucleotide sequences that have about 70% or 95% sequence identity to instant

SEQ ID NO: 11 are not described, and thus their function is unknown.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient elements of a FMT protein of SEQ ID NO: 12. Thus, Applicant's broadly claimed genus encompasses structures whose function is unrelated to the instantly claimed SEQ ID NO: 11 encoding the FMT protein of SEQ ID NO: 12.

The only species described in the specification is SEQ ID NO: 11, which encodes SEQ ID NO: 12.

It is, therefore, maintained that one of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NOs: 11 and 12 are insufficient to describe the claimed genus.

The essential feature of newly added claims 92, 100 and 103 is a nucleotide sequence which is capable of hybridizing under medium stringency conditions to a nucleotide sequence encoding the protein of SEQ ID NO: 12.

The essential feature of newly claims 92, 100 and 103 is also a nucleotide sequence which hybridizes under medium stringency conditions to a nucleotide sequence of SEQ ID NO: 11, or hybridizes under medium stringency conditions to a nucleotide sequence which encodes a protein having at least about 80% sequence similarity to SEQ ID NO: 12.

The medium stringency conditions of hybridization as described on page 28 of specification would encompass hybridization of nucleotide sequences that are unrelated in structure and function to a nucleotide sequence encoding the functional FMT protein of SEQ ID NO: 12.

The specification does not describe the structure and function of said unrelated hybridizing sequences.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient elements of a nucleic acid sequence which encodes SEQ ID NO: 12.

The only species described in the specification is SEQ ID NO: 11, which encodes SEQ ID NO: 12.

Structures that would hybridize under medium stringency conditions to a nucleotide sequence (including SEQ ID NO: 11) encoding SEQ ID NO: 12 are not described, and thus their function is unknown.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 11 and its encoded protein of SEQ ID NO: 12 are insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described the following: (a) nucleotide sequences having about 70% or 95% sequence identity to SEQ ID NO: 11, (b) nucleotide sequences encoding proteins having about 80% or 95% sequence identity to

SEQ ID NO: 12, and (d) nucleotide sequences which hybridize under medium stringency conditions to a nucleotide sequence encoding SEQ ID NO: 12, and the specification fails to provide an adequate written description of the claimed invention.

Accordingly, it is maintained that there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written Description guidelines published in Federal Register/Vol.66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide written description of the genus broadly claimed. Accordingly, it is maintained that one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing.

Also see in re Curtis (69 USPQ2d 1274 (Fed. Cir.2004), where the court held that there was sufficient evidence to indicate that one of ordinary skill in the art could not predict the operability of other species other that the single one disclosed in the specification. The court held that a disclosure naming a single species can support a claim to a genus that includes that species if a person of ordinary skill in the art, reading the initial disclosure, would "instantly recall" additional species of the genus already "stored" in the minds, but if other members of the genus would not "naturally occur" to a person of ordinary skill upon reading the disclosure, then unpredictability in performance of species other than specifically enumerated defeats claims to the genus.

For at least these reasons and the reasons of record stated in the previous Office Action, the requirement for written description has not been met. Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 102

16. Newly added claims 92 and 95-100 are rejected under 35 U.S.C. 102(b) as being anticipated by Gauthier et al. (GenBank Sequence Accession No. U16794, pages 1-2, published November 8, 1995) taken with the evidence of Joshi et al. (Plant Molecular Biology, 37:663-674, 1998, Applicant's IDS) for the reasons of record stated for claims 70-79 (now cancelled) in the Office action of March 17, 2008. Applicant traverses the rejection in the paper filed September 17, 2008.

Applicant argues that Gauthier et al. do not teach a nucleic acid that encodes a FMT, and that is characterized by the currently recited sequence and hybridization features (response, pg 12, 4th paragraph).

Applicant's arguments have been fully considered but are deemed to be unpersuasive.

It is maintained that Gauthier et al. disclose a cDNA clone comprising a genetic construct, which comprises a cDNA sequence encoding 3' flavonoid O-methyltransferase protein (pg 2). The reference further discloses that said cDNA clone was isolated from cDNA expression library (Uni-Zap XR, see pg 1 under features, line 32). The reference further discloses that said library was prepared from

Chrysosplenium americanum (pg 1, line 27). The reference also discloses 3' flavonoid O-methyltransferase activity of the protein disclosed in the reference (pg 1, lines 38 and 43, experimental results).

It is important to note that since cDNA clone disclosed in the reference was isolated from a cDNA expression library, it would thus inherently comprise other components of a genetic construct, such as, a promoter and transcription termination signals.

Although Gauthier et al. do not explicitly disclose that their FMT protein is a class I S-adenosyl-L-methionine *O*-methytransferase which acts on anthocyanin molecule, such a feature is inherent to the FMT protein disclosed by Gauthier et al. This is further evidenced by Joshi et al., who disclose a 3' flavonoid *O*-methyltransferase sequence (GenBank accession No. U16794, pg 665, table 1) having 100% sequence identity to Gauthier et al. FMT, and which methylates (same as "acts on") anthocyanin (flavonoids) substrates. Joshi et al. also disclose that their 3' flavonoid O-methyltransferase is a S-adenosyl-L-methionine O-methyltransferase. See in particular, page 664, 2nd paragraph of right column; page 665, table 1; page 665 tables 1-2; page 668, table 4; pages 670-671, figure 2).

Although Gauthier et al. do not explicitly disclose methylation property of 3' flavonoid *O*-methyltransferase on anthocyanins substrates, such as, delphinidin, delphinidin-3-glucoside (derivative of delphinidin), petunidin or petunidin derivatives, such a property would be inherent to the enzymatic activity of Gauthier et al. 3' flavonoid *O*-methyltransferase, unless the Applicant provides evidence to the contrary.

This rejection is made because of the following reason:

The "medium stringency conditions" recited in claims 92 and 100 would encompass hybridization of a nucleotide sequence having low homology to a nucleotide sequence encoding SEQ ID NO: 12, and encoding a functional flavonoid methyltransferase. In the instant case, Gauthier et al. cDNA sequence would be able to hybridize under "medium stringency conditions" recited in instant claims (92 or 101) to a nucleotide sequence (including SEQ ID NO: 11) encoding instant SEQ ID NO: 12.

Accordingly, Gauthier et al. anticipated the claimed invention.

Claim Rejections - 35 USC § 103

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Newly added claims 92, 95-100, 103 and 106-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jorgensen et al. (US Patent No. 5,034,323, Issued July 23, 1991), in view of Joshi et al. (Plant Molecular Biology, 37:663-674, 1998, Applicant's IDS), and Jonsson et al. (Planta, 160:174-179, 1984) for the reasons of record stated for claims 70-89 (now cancelled) in the Office action of March 17, 2008.

Applicant traverses the rejection in the paper filed September 17, 2008.

Applicant argues that Joshi et al. do not teach a nucleic acid that encodes a FMT, and that is characterized by the currently recited sequence and hybridization features (response, pg 13, 2nd paragraph).

Applicant's arguments have been fully considered but are deemed to be unpersuasive.

It is maintained that Jorgensen et al. teach a method of making a genetically modified transformed plant, comprising transformation of said plant with a nucleotide sequence encoding an anthocyanin biosynthetic enzyme (CS). The reference also teaches a plant transformation vector comprising a genetic construct having said nucleotide sequence operably linked to a promoter, and using said construct in obtaining the genetically transformed plant. The reference further teaches that the genetically modified transformed plant exhibited increase in anthocyanin levels in its flowers. See in particular, columns 13-16, example 1; columns 17-20, examples 2-4; claims 1-5.

The reference also teaches that flower color and morphology can be altered by manipulating the gene expression of flavonoid methyltransferases (e.g. flavonoid 3' or 3',5'-O-methyltransferases). See in particular, column 4, lines 40-68. The reference further teaches a number of target plants that can be genetically modified with said flavonoid methyltransferases. These include cut flower and/or horticultural plant

species, such as, roses, lilies, petunias etc., and agricultural plant species, such as, potato, radishes, eggplants, cauliflower etc. (see column 8, lines 44-59).

Jorgensen et al. do not teach a genetically modified plant comprising a nucleotide sequence encoding a flavonoid methyltransferase (FMT).

It is maintained that Joshi et al. teach a large number of flavonoid methyltransferase protein sequences. The reference also teach a GenBank sequence accession No. U16794 (pg 665, table 1) encoding 3' flavonoid O-methyltransferase which is a S-adenosyl-L-methionine O-methyltransferase. The reference further teaches that said methyltransferase methylates (same as "acts on") anthocyanin (flavonoid) substrates. See in particular, page 664, 2nd paragraph of right column; page 665, table 1; page 665 tables 1-2; page 668, table 4; pages 670-671, figure 2).

It is maintained that Jonsson et al. teach 3' or 5' methylation activity of a 3'/5' FMT (S-adenosyl-L-methionine O-methyltransferase) protein on anthocyanin substrates (same as molecules). These substrates include: delphinidin, cyanidin, petunidin or derivatives thereof, or delphinidin 3-glucoside (derivative of delphinidin). See in particular, page 174, abstract, paragraph bridging left and right columns; page 175, table 1, figure 1; page 176, figures 2-3; page 177, table 2; page 178, figures 4 and 5.

The reference further teaches that methylated anthocyanins increases attraction (due to attractive flower color and morphology) of pollinators and methylation of anthocyanins increases lipid solubility of flavonoid compounds which is advantageous for subcellular transport to the vacuole, where the anthocyanins accumulate. The reference further teaches that methylation increases stability of anthocyanin molecules

by masking the reactive phenolic groups. The reference also teaches that increased anthocyanin stability results in increased anthocyanin accumulation (see page 179, left column, lines 22-36).

At the time the invention was made, it would have been prima facie obvious and within the scope of an ordinary skill in the art to modify the method of modifying anthocyanin content in a plant as taught by Jorgensen et al., to substitute the nucleotide sequence encoding an anthocyanin biosynthesis enzyme of Jorgensen et al. with a nucleic acid sequence encoding Joshi et al. flavonoid methyltransferase to obtain a genetically modified transgenic plant expressing Joshi et al. flavonoid methyltransferase with reasonable expectation of success.

Given that Jonsson et al. teach that methylation of anthocyanins (including derivatives of anthocyanins) by a functional flavonoid methyltransferase increases accumulation of anthocyanins and derivatives thereof, and which results in increased attraction towards pollinators, it would have been obvious and within the scope of an ordinary skill in the art to over-express any functional flavonoid methyltransferase including the one taught by Joshi et al. in any genetically modified flowering crop (agricultural plant) plant. One of ordinary skill in the art would have been motivated to do so because increased pollination due to high anthocyanin levels would have resulted in higher seed set and thus accounted for increase in yield with reasonable expectation of success.

Given that Jonsson et al. teach that methylation of anthocyanins (including derivatives of anthocyanins) by a functional flavonoid methyltransferase increases

accumulation of anthocyanins and derivatives thereof, and which results in attractive flower colors and inflorescence, it would have been obvious and within the scope of an ordinary skill in the art to over-express any functional flavonoid methyltransferase including the one taught by Joshi et al. in any genetically modified horticultural (e.g. an ornamental) plant species. One of ordinary skill in the art would have been motivated to do so for the purpose of obtaining a transgenic ornamental (horticultural) plant species exhibiting an altered inflorescence having attractive colored flower parts, such as sepals, petals etc. with reasonable expectation of success.

Obviously propagation material, such as seeds, progenies or cuttings would have been produced for the purpose of propagation of said genetically modified transgenic plants.

This rejection is made because of the following reasons:

The "medium stringency conditions" recited in claims 92, 100 and 103 would encompass hybridization of a nucleotide sequence having low homology to a nucleotide sequence encoding SEQ ID NO: 12, and encoding a functional flavonoid methyltransferase. In the instant case, Joshi et al. cDNA sequence taught in GenBank sequence accession No. U16794 would be able to hybridize under "medium stringency conditions" recited in instant claims (92, 100 and 103) to a nucleotide sequence (including SEQ ID NO: 11) encoding instant SEQ ID NO: 12.

Thus, the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

Conclusions

18. Newly added claims 92-113 are rejected. Newly added claims 93-94, 101-102 and 104-105 are free from prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)272-0975. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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/Phuong T. Bui/
Primary Examiner, Art Unit 1638